REMARKS

Claims 1, 5-22, 26 and 31-34 are pending in the application. Claims 2-4 and 35 have been canceled without prejudice and claims 23-25 and 27-29 are withdrawn.

Applicants submit these amendments in view of the Advisory Action mailed November 19, 2003, in which the Examiner stated that entry of the amendments filed October 3, 2003 would raise new 35 USC 112 rejections. He alleges it would be confusing and unclear whether claim 10 would be limiting the "selective markers" of claim 9 or the "selectable markers" of claim 1, as amended. Applicants have replaced the phrase "selectable markers" with "selective markers" in the amendment to claim 1, obviating the Examiner's basis for non-entry of the amendments. Entry of the amendments is respectfully requested.

I. Support for Claim Amendments

The claims were amended to more clearly define the invention. Claims 1, 21, and 26 were amended to recite that the recombinant DNA is an expression vector comprising at least one protein. The protein is encoded by a homologous or heterologous coding sequence selected from the group consisting of heparinase I, heparinase II, heparinase III, and selective markers. Support for these amendments are found throughout the Specification, for example, on pages 11-12. Accordingly, no new matter is added by this Amendment and entry thereof is respectfully requested.

II. Objection to Claim 1

The Examiner objected to claim 1 because of informality in the language of the claim. Applicants have amended this claim as suggested by the Examiner.

III. Rejection of claims 1-22, 26 and 30-35 under 35 U.S.C. § 112, first paragraph

Claims 1-22, 26, and 30-35 are rejected under 35 U.S.C. § 112, first paragraph, as the claims allegedly contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner rejected the claims because he alleges that they "include all *Flavobacterium heparinum* host cells transformed with any recombinant DNA construction effective to cause expression of any protein." Further, the Examiner states that "Applicants invention of a new host system for expressing DNA is recognized, however applicants new host system is not representative of any host system which employs any *Flavobacterium heparinum* host cells transformed with any recombinant DNA construction effective to cause expression of any protein."

Applicants appreciate the Examiner's recognition of their invention of a new host system for expressing DNA. Independent claims 1, 21, and 26, and claims 5-20, 22, and 31-34 dependent thereon, were amended to recite a *Flavobacterium heparinum* host transformed with an expression vector effective to cause expression of at least one of heparinase I, heparinase II, heparinase III, or a selective markers. Claims 2-4 and 35 have been canceled. Applicants respectfully submit that the claims fully comply with the guidelines for written description required by 35 U.S.C. § 112, first paragraph. It is clear from the disclosure in the Specification that Applicants are in possession of the claimed invention, a new *Flavobacterium heparinum*

host system for expressing heparinase enzymes or selective markers using expression vectors. Examples 1 and 2 on pages 8-9 of the Specification describe construction of expression vectors for expression of both homologous genes and heterologous genes in the *Flavobacterium heparinum* host cell. Example 4 on page 11 of the Specification describes the expression of heparinase I, heparinase II, heparinase III, and selective markers by the *F. heparinum* host transformed with the expression vectors.

The Examiner has further rejected claims 1-22, 26, and 30-35 under 35 U.S.C. § 112, first paragraph, for lack of enabling disclosure. The Examiner asserts that the Specification does not reasonably provide an enabling disclosure for *Flavobacterium heparinum* transformed with any vector. Applicants respectfully traverse the rejection. Applicants have provided a complete and enabling disclosure of their invention, as recognized by the Examiner to be a new host system for expressing DNA. As set forth above, the Specification and the Examples teach and demonstrate to one having skill in the art how to make the expression vectors of the present invention and how to obtain expression in the *F. heparinum* host. Nevertheless, Applicants have amended the claims to recite a *Flavobacterium heparinum* host transformed with an expression vector effective to cause expression of at least one of heparinase I, heparinase II, heparinase III, or selective markers. Applicants submit that these amendments obviate the instant rejection for the reasons discussed in the foregoing paragraph. Withdrawal of the rejection of claims 1, 5-22, 26, and 30-34 under 35 U.S.C. § 112, first paragraph, is respectfully requested.

IV. Rejection of claims 1-11, 13-21, 26, and 30-35 under 35 U.S.C. § 103(a)

Claims 1-11, 13-21, 26, and 30-35 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Zimmerman et al. (WO 96/01894, January 25, 1996) and McBride et al. (Applied and Environmental Microbiology, Vol. 62, No. 8, pages 3017-3022, August 1996). Zimmerman et al. is relied on for teaching the culturing of *Flavobacterium heparinum* and the isolation and cloning of the genes encoding the enzymes, chondroitinase AC and chondroitinase B, from *Flavobacterium heparinum.* Zimmerman et al. is further relied upon to teach that the cloned genes can be used in conjunction with suitable expression systems to produce enzymes in *Flavobacterium*, for example, under the control of overexpression promoters, or in organisms other than *Flavobacterium.* McBride et al. is relied on for using the tn4351 transposon to introduce heterologous DNA into *Flavobacterium meningosepticum*, activities which the Examiner alleges provides a reasonable expectation of success for the *Flavobacterium heparinum* expression system as suggested by Zimmerman et al. The Examiner concludes that one of ordinary skill in the art at the time of the filing would have been motivated to express the genes encoding the *Flavobacterium heparinum* enzymes, chondroitinase AC and chondroitinase B, in *Flavobacterium heparinum* under the control of an overexpression promoter in a suitable expression system, such as the tn4351 transposon DNA, as taught by McBride at al. and suggested by Zimmerman et al. Applicants respectfully traverse this rejection.

Independent claims 1, 21, and 26, and claims 5-11, 13-20, and 30-34 dependent thereon, as amended, recite a *Flavobacterium heparinum* host transformed with an expression vector effective to cause expression of at least one of heparinase I, heparinase II, heparinase III, or a selective marker. Claims 2-4 and 35 have been canceled. Applicants respectfully submit that

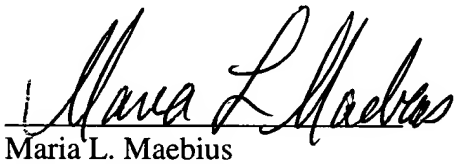
these claims are not rendered obvious by the combination of Zimmerman and McBride references. In order to establish a *prima facie* case of obviousness under 103(a), all claim limitations must be taught or suggested by the prior art. The use of expression vectors for expression of heparinase I, heparinase II, heparinase III, or a selective marker in a *F. heparinum* host is not taught or suggested by either Zimmerman or McBride, alone or in combination. The Examiner alleges that Zimmerman and McBride would have motivated one of ordinary skill in the art at the time of filing to express the genes encoding the *Flavobacterium heparinum* enzymes, chondroitinase AC and chondroitinase B, in *Flavobacterium heparinum* under the control of an overexpression promoter in a suitable expression system, such as the tn4351 transposon DNA. What Applicants are teaching is the expression of homologous or heterologous gene sequences encoding at least one of heparinase I, heparinase II, heparinase III, or a selective marker in *Flavobacterium heparinum* in an expression system using expression vectors, not the tn4351 transposon DNA. In fact, the inventors attempted to transfer DNA into *F. heparinum* via a transposon but were not able to obtain DNA integration, as shown in the attached Su et al., *Microbiology* 147: 581-589 (2001) reference. In particular, the authors state that previous attempts to use transposons into *F. heparinum* failed. *See* page 585, col. 2, first full paragraph. Accordingly, the combination of Zimmerman and McBride cannot establish a *prima facie* case of obviousness.

Applicants submit that the claimed invention is not rendered obvious by Zimmerman and McBride because the references do not teach or suggest all the limitations of the claimed invention. Withdrawal of the rejection of claims 1, 5-11, 13-21, 26 and 30-34 under 35 U.S.C. § 103(a) is respectfully requested.

IX. CONCLUSION

In view of the foregoing remarks, Applicants believe that the application is in condition for allowance. However, if the Examiner disagrees, he is encouraged to call the undersigned at the number listed below in order to expedite the prosecution of this application.

Respectfully submitted,



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